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GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: SCHIZOPHRENIA ASSOCIATED GENES

(57) Abstract: The present invention relates to the identification of genes which have been disrupted in patients diagnosed as suf-
fering from schizophrenia and/or bi-polar affective disorder, as well as proteins encoded by the gene and antibodies thereto and to
uses of such products as medicaments for treating schizophrenia and/or affective psychosis. The invention also relates to methods
for diagnosing patients suffering or predisposed to schizophrenia and/or affective psychosis, as well as screens for developing novel
treatment regimes for schizophrenia and/or affective psychosis.



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INTERNATIONAL SEARCH REPORT

International Application No

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68 A61K38/00 A61K48/00 A61K39/395 A01K67/027
G01N33/53

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE

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A	WO 01 40301 A (MEDICAL RES COUNCIL (GB)) 7 June 2001 (2001-06-07) page 1, line 27 -page 2, line 14 page 3, line 10 -page 4, line 26 page 9, line 10 -page 10, line 19 ---	1,2,8,9, 14-23
A	WO 00 58510 A (GENSET SA (FR)) 5 October 2000 (2000-10-05) claims 1,9,40,61,64 --- -/--	1,2,8,9, 14-23

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

5 February 2004

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03. 03. 2004

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INTERNATIONAL SEARCH REPORT

Inte at Application No
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A	-& DATABASE GSN [Online] 11 January 2002 (2002-01-11) TANG Y.T. ET AL.: "Human semaphorin domain-associated protein homologue cDNA, SEQ: 724" Database accession no. ABA08948 XP002259172 abstract	1,2,8,9, 14-23
A	WO 01 53455 A (HYSEQ INC) 26 July 2001 (2001-07-26) SEQ ID NO:496; SEQ ID NO:1235	1,2,8,9, 14-23
A	KIKUNO R ET AL: "PREDICTION OF THE CODING SEQUENCES OF UNIDENTIFIED HUMAN GENES. XIV. THE COMPLETE SEQUENCES OF 100 NEW CDNA CLONES FROM BRAIN WHICH CODE FOR LARGE PROTEINS IN VITRO" DNA RESEARCH, vol. 6, 1999, pages 197-205, XP000852618 ISSN: 1340-2838 tables 1,2	1,2,8,9, 14-23
X	WO 01 51659 A (GENSET SA) 19 July 2001 (2001-07-19) This document refers to invention 2 SEQ ID NO:544	1,3,8, 10,14-23
A	WO 95 32214 A (CANJI INC) 30 November 1995 (1995-11-30) This document refers to invention 2 and invention 6 figures 10,14,12	1,3,8, 10,14-23
A	DATABASE EM EST [Online] 24 December 2000 (2000-12-24) NIH-MGC: "602121812F1 NIH MGC 56 Homo sapiens cDNA clone IMAGE:4278939 5', mRNA sequence" Database accession no. BF667452 XP002269196 This document refers to invention 2 abstract	1,3,8, 10,14-23
A	EP 0 529 994 A (ALLELIX BIOPHARMA) 3 March 1993 (1993-03-03) This document refers to invention 3 figure 1	1,4,8, 11,14-23

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 03/01543

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X	<p>SOKOLOV BORIS P: "Expression of NMDAR1, GluR7, and KA1 glutamate receptor mRNAs is decreased in frontal cortex of "neuroleptic-free" schizophrenics: Evidence on reversible up-regulation by typical neuroleptics" JOURNAL OF NEUROCHEMISTRY, vol. 71, no. 6, December 1998 (1998-12), pages 2454-2464, XP002269194 ISSN: 0022-3042 This document refers to invention 3 page 2458, column 1, paragraph 3 -column 2, paragraph 1 page 2460, column 2, paragraph 4 -page 2461, column 1, paragraph 1; table 2.</p>	1,4,8, 11,14-23
X	<p>BISCHOFF SERGE ET AL: "Spatial distribution of kainate receptor subunit mRNA in the mouse basal ganglia and ventral mesencephalon" JOURNAL OF COMPARATIVE NEUROLOGY, vol. 379, no. 4, 1997, pages 541-562, XP008027199 ISSN: 0021-9967 5 last lines of the abstract This document refers to invention 3 page 559, line 22 - line 28</p>	1,4,6, 11,14-18
A	<p>WO 99 28464 A (WISCONSIN ALUMNI RES FOUND (US)) 10 June 1999 (1999-06-10) This document refers to invention 4 SEQ ID NO:6; SEQ ID NO:15</p>	1,5,8, 14-23
A	<p>DATABASE EM HUM [Online] 30 November 2000 (2000-11-30) THOMAS R.S. ET AL.: "Homo sapiens basic-helix-loop-helix-PAS protein (MOP6) mRNA, complete cds." Database accession no. AF164438 XP002269197 This document refers to invention 4 abstract</p>	1,5,8, 14-23
P,A	<p>WO 03 025138 A (EOS BIOTECHNOLOGY INC) 27 March 2003 (2003-03-27) This document refers to invention 4 SEQ ID NO:143 page 705 -page 707</p>	1,5,8, 14-23

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In Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	KAMNASARAN D. ET AL: "Disruption of the neuronal PAS3 gene in a family affected with schizophrenia." JOURNAL OF MEDICAL GENETICS, vol. 40, no. 5, May 2003 (2003-05), pages 325-332, XP008027189 ISSN: 0022-2593 This document refers to invention 4 the whole document	1,5,8, 14-23
A	US 5 977 305 A (COLICELLI JOHN J ET AL) 2 November 1999 (1999-11-02) This document relates to invention 5 SEQ ID NO:23; SEQ ID NO:58	1,6,8, 12,14-23
A	US 6 323 041 B1 (ROBBINS MICHAEL D ET AL) 27 November 2001 (2001-11-27) This document relates to invention 5 SEQ ID NO:1-3 figures 2A,B	1,6,8, 12,14-23
A	DATABASE GSN [Online] 28 July 2000 (2000-07-28) NYCE JW: "Human adenosine receptor related polynucleotide SEQ ID NO:2605" Database accession no. AAA34916 XP002269198 abstract	1,6,8, 12,14-23
A	& WO 00 09525 A (UNIV EAST CAROLINA (US)) 24 February 2000 (2000-02-24) This document refers to invention 5 SEQ ID NO:2605	1,6,8, 12,14-23
A	BOLGER G. ET AL.: "A FAMILY OF HUMAN PHOSPHODIESTERASES HOMOLOGOUS TO THE DUNCE LEARNING AND MEMORY GENE PRODUCT OF DROSOPHILA MELANOGASTER ARE POTENTIAL TARGETS FOR ANTIDEPRESSANT DRUGS" MOLECULAR AND CELLULAR BIOLOGY, vol. 13, no. 10, 1 October 1993 (1993-10-01), pages 6558-6571, XP000566626 This document refers to invention 5 figure 2A	1,6,8, 12,14-23
A	SHIMOYAMA Y. ET AL.: "Identification of three human type-II classic cadherins and frequent heterophilic interactions between different subclasses of type-II classic cadherins" BIOCHEMICAL JOURNAL, vol. 349, no. 1, 1 July 2000 (2000-07-01), pages 159-167, XP002269195 This document refers to invention 6 figure 1	1,7,8, 13-23

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INTERNATIONAL SEARCH REPORT

Inte Application No
PCT/03/01543

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>DATABASE GSP [Online] 18 February 2002 (2002-02-18) DRMANAC RT: "Novel human diagnostic protein #12390" Database accession no. ABG12399 XP002269199 abstract</p>	<p>1,7,8, 13-23</p>
A	<p>& WO 01 75067 A (HYSEQ INC) 11 October 2001 (2001-10-11) This document refers to invention 6 SEQ ID NO:42758 -----</p>	<p>1,7,8, 13-23</p>

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International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-14 (searched incompletely)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 2,9 (completely); 1,8,14-23 (partially)

Use of a polynucleotide or polypeptide fragment of SEMCAP3 for the manufacture of a medicament for treating schizophrenia and/or affective psychosis; a method of diagnosing said diseases in an individual; use of an antibody specific for SEMCAP3 for diagnosis of said diseases or for the manufacture of a medicament for the treatment of said diseases; an animal model wherein expression of SEMCAP3 is specifically disrupted or upregulated; a method for identifying ligands for SEMCAP3.

2. Claims: 3,10 (completely); 1,8,14-23 (partially)

Use of a polynucleotide or polypeptide fragment of N33 for the manufacture of a medicament for treating schizophrenia and/or affective psychosis; a method of diagnosing said diseases in an individual; use of an antibody specific for N33 for diagnosis of said diseases or for the manufacture of a medicament for the treatment of said diseases; an animal model wherein expression of N33 is specifically disrupted or upregulated; a method for identifying ligands for N33.

3. Claims: 4,11 (completely); 1,8,14-23 (partially)

Use of a polynucleotide or polypeptide fragment of GRIK4 for the manufacture of a medicament for treating schizophrenia and/or affective psychosis; a method of diagnosing said diseases in an individual; use of an antibody specific for GRIK4 for diagnosis of said diseases or for the manufacture of a medicament for the treatment of said diseases; an animal model wherein expression of GRIK4 is specifically disrupted or upregulated; a method for identifying ligands for GRIK4.

4. Claims: 5 (completely); 1,8,14-23 (partially)

Use of a polynucleotide fragment of NPAS3 for the manufacture of a medicament for treating schizophrenia and/or affective psychosis; a method of diagnosing said diseases in an individual; use of an antibody specific for NPAS3 for diagnosis of said diseases or for the manufacture of a medicament for the treatment of said diseases; an animal model wherein expression of NPAS3 is specifically disrupted or upregulated; a method for identifying ligands for NPAS3.

5. Claims: 6,12 (completely); 1,8,14-23 (partially)

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Use of a polynucleotide or polypeptide fragment of PDE4B for the manufacture of a medicament for treating schizophrenia and/or affective psychosis; a method of diagnosing said diseases in an individual; use of an antibody specific for PDE4B for diagnosis of said diseases or for the manufacture of a medicament for the treatment of said diseases; an animal model wherein expression of PDE4B is specifically disrupted or upregulated; a method for identifying ligands for PDE4B.

6. Claims: 7,13 (completely); 1,8,14-23 (partially)

Use of a polynucleotide or polypeptide fragment of CDH8 for the manufacture of a medicament for treating schizophrenia and/or affective psychosis; a method of diagnosing said diseases in an individual; use of an antibody specific for CDH8 for diagnosis of said diseases or for the manufacture of a medicament for the treatment of said diseases; an animal model wherein expression of CDH8 is specifically disrupted or upregulated; a method for identifying ligands for CDH8.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I:2

Claims Nos.: 1-14 (searched incompletely)

Please note that the following objections refer to claims 1-14, although only the claims of the 1st invention have been searched (claims 2,9 (completely); claims 1,8,14-23 (partially)):

Present claims 1,8 and dependent claims relate to an extremely large number of possible polynucleotides and polypeptides due to the expression "...fragments, derivatives or homologues thereof...", whereby the application documents provide no definition for the terms "derivative" or "homologue" and only an extremely broad definition for the term "fragment" (even a single nucleotide is included in this definition). In fact, the claims contain so many options, that a lack of clarity and conciseness within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear, namely the use of the full-length sequences of the mentioned polynucleotides or polypeptides of claim 1 and 8 and the use of the specific polynucleotides or polypeptides mentioned in the figures as referred to in claims 2-7 and 9-13.

Present claims 2-7 and 9-13 refer inter alia to the use of polynucleotides and polypeptides defined by a database accession number. No search can be performed for the use of these polynucleotides and polypeptides for the following reasons:

1) Art. 15(3), PCT states: "International search shall be made on the basis of the claims, with due regard to the description and the drawings (if any)". Since the sequence information is not contained in the claims, description or drawings, but said information can only be retrieved by accessing a database, the sequence information is not part of the application documents.

2) The information contained in a database record can be changed continuously, theoretically even uncontrolled, which implies that it cannot be determined with absolute certainty whether the information in the database record is the same as the information at the time of filing of the application. Therefore, disclosing a sequence by way of referring to a database record inherently creates a legal uncertainty as the integrity of the data over time cannot be guaranteed and thus the requirements of Art. 5 PCT have not been fulfilled.

Consequently, the search for the above mentioned claims has been carried out for the use of clearly defined polynucleotides and polypeptides, which are disclosed in the application documents, i.e. for the use of polynucleotides and polypeptides as mentioned in the figures as referred to in claims 2-7 and 9-13.

Furthermore, present claim 14 relates to the use of an extremely large number of possible polynucleotides and polypeptides due to the expression "...consisting essentially of...". In fact, the claim contains so many options that a lack of clarity and conciseness within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

for those parts of the application which do appear to be clear namely to the use of the identified sequences.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter application No

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Information on patent family members

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